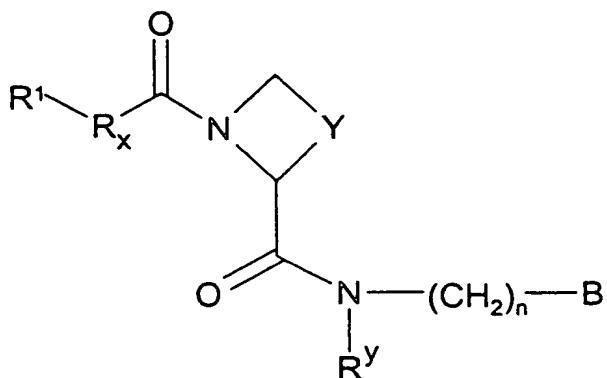


## Claims

1. A compound of formula I,



5

wherein

R<sup>1</sup> represents H, C<sub>1-4</sub> alkyl (optionally substituted by one or more substituents selected from cyano, halo, OH, C(O)OR<sup>1a</sup> or C(O)N(R<sup>1b</sup>)R<sup>1c</sup>) or OR<sup>1d</sup>;

R<sup>1d</sup> represents H, C(O)R<sup>11</sup>, SiR<sup>12</sup>R<sup>13</sup>R<sup>14</sup> or C<sub>1-6</sub> alkyl, which latter group is optionally substituted or terminated by one or more substituent selected from OR<sup>15</sup> or (CH<sub>2</sub>)<sub>q</sub>R<sup>16</sup>;

15 R<sup>12</sup>, R<sup>13</sup> and R<sup>14</sup> independently represent H, phenyl or C<sub>1-6</sub> alkyl;

R<sup>16</sup> represents C<sub>1-4</sub> alkyl, phenyl, OH, C(O)OR<sup>17</sup> or C(O)N(H)R<sup>18</sup>;

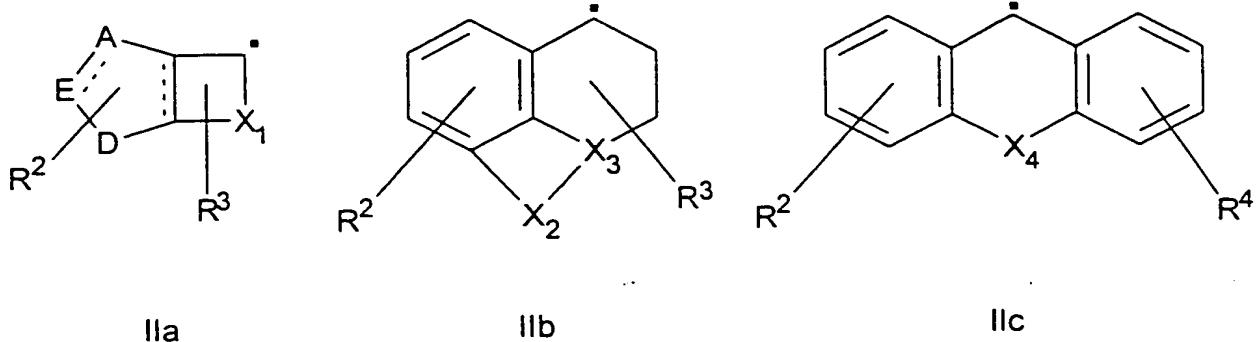
R<sup>18</sup> represents H, C<sub>1-4</sub> alkyl or CH<sub>2</sub>C(O)OR<sup>19</sup>;

R<sup>15</sup> and R<sup>17</sup> independently represent H, C<sub>1-6</sub> alkyl or C<sub>1-3</sub> alkylphenyl;

R<sup>1a</sup>, R<sup>1b</sup>, R<sup>1c</sup>, R<sup>11</sup> and R<sup>19</sup> independently represent H or C<sub>1-4</sub> alkyl; and

20 q represents 0, 1 or 2;

$R_x$  represents a structural fragment of formula IIa, IIb or IIc,



5 wherein

the dotted lines independently represent optional bonds;

A and E independently represent O or S, CH or  $CH_2$  (as appropriate), or N or  $N(R^{21})$  (as appropriate);

D represents  $-CH_2-$ , O, S,  $N(R^{22})$ ,  $-(CH_2)_2-$ ,  $-CH=CH-$ ,  $-CH_2N(R^{22})-$ ,

10  $-N(R^{22})CH_2-$ ,  $-CH=N-$ ,  $-N=CH-$ ,  $-CH_2O-$ ,  $-OCH_2-$ ,  $-CH_2S-$  or  $-SCH_2-$ ;

$X_1$  represents  $C_{2-4}$  alkylene;  $C_{2-3}$  alkylene interrupted by Z;  $-C(O)-Z-A^1-$ ;

$-Z-C(O)-A^1-$ ;  $-CH_2-C(O)-A^1-$ ;  $-Z-C(O)-Z-A^2-$ ;  $-CH_2-Z-C(O)-A^2-$ ;

$-Z-CH_2-C(O)-A^2-$ ;  $-Z-CH_2-S(O)_m-A^2-$ ;  $-C(O)-A^3$ ;  $-Z-A^3-$ ; or  $-A^3-Z-$ ;

$X_2$  represents  $C_{2-3}$  alkylene,  $-C(O)-A^4-$  or  $-A^4-C(O)-$ ;

15  $X_3$  represents CH or N;

$X_4$  represents a single bond, O, S, C(O),  $N(R^{23})$ ,  $-CH(R^{23})-$ ,

$-CH(R^{23})-CH(R^{24})-$  or  $-C(R^{23})=C(R^{24})-$ ;

$A^1$  represents a single bond or  $C_{1-2}$  alkylene;

$A^2$  represents a single bond or  $-CH_2-$ ;

20  $A^3$  represents  $C_{1-3}$  alkylene;

$A^4$  represents C(O) or  $C_{1-2}$  alkylene;

Z represents, at each occurrence, O,  $S(O)_m$  or  $N(R^{25})$ ;

$R^2$  and  $R^4$  independently represent one or more optional substituents

selected from  $C_{1-4}$  alkyl,  $C_{1-4}$  alkoxy (which latter two groups are optionally substituted by one or more halo substituent), methylenedioxy, halo, hydroxy, cyano, nitro,  $S(O)_2NH_2$ ,  $C(O)OR^{26}$ ,  $SR^{26}$ ,  $S(O)R^{26a}$ ,  $S(O)_2R^{26a}$  or  $N(R^{27})R^{28}$ ;

5      $R^3$  represents one or more optional substituents selected from OH,  $C_{1-4}$  alkoxy,  $C_{1-6}$  alkyl (optionally substituted by one or more halo group), or  $N(R^{29a})R^{29b}$ ;

$R^{25}$ ,  $R^{29a}$  and  $R^{29b}$  independently represent H,  $C_{1-4}$  alkyl or  $C(O)R^{30}$ ;

$R^{26}$  represents H or  $C_{1-4}$  alkyl;

10     $R^{26a}$  represents  $C_{1-4}$  alkyl;

$R^{27}$  and  $R^{28}$  independently represent H,  $C_{1-4}$  alkyl or  $C(O)R^{30}$ , or together represent  $C_{3-6}$  alkylene, thus forming a 4- to 7-membered ring, which ring is optionally substituted, on a carbon atom that is  $\alpha$  to the nitrogen atom, with an =O group;

15     $R^{21}$ ,  $R^{22}$ ,  $R^{23}$ ,  $R^{24}$  and  $R^{30}$  independently represent, at each occurrence, H or  $C_{1-4}$  alkyl;

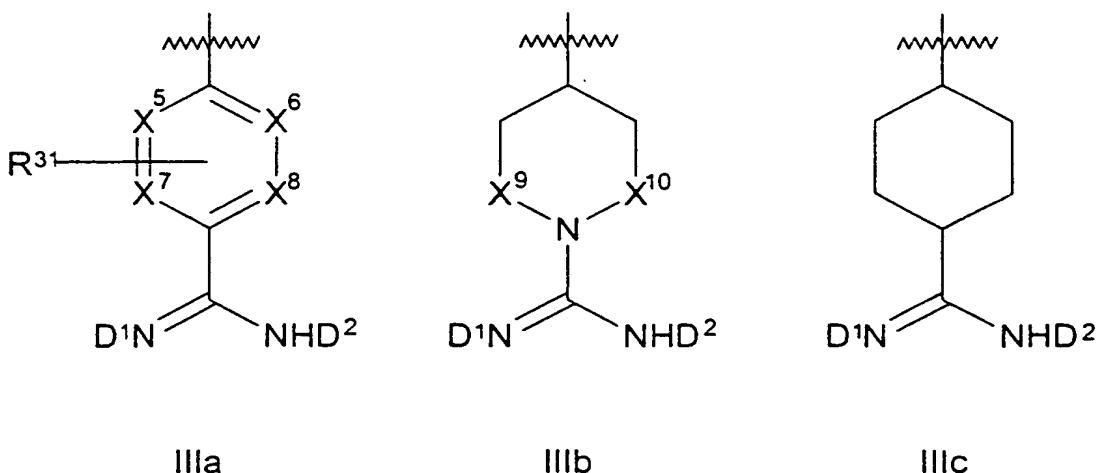
Y represents  $CH_2$ ,  $(CH_2)_2$ ,  $CH=CH$  (which latter group is optionally substituted by  $C_{1-4}$  alkyl),  $(CH_2)_3$ ,  $CH_2CH=CH$  or  $CH=CHCH_2$  (which

20    latter three groups are optionally substituted by  $C_{1-4}$  alkyl, methylene, =O or hydroxy);

$R^y$  represents H or  $C_{1-4}$  alkyl;

25    n represents 0, 1, 2, 3 or 4; and

B represents a structural fragment of formula IIIa, IIIb or IIIc



wherein

X<sup>5</sup>, X<sup>6</sup>, X<sup>7</sup> and X<sup>8</sup> independently represent CH, N or N-O;

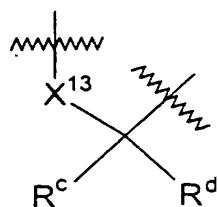
X<sup>9</sup> and X<sup>10</sup> independently represent a single bond or CH<sub>2</sub>;

5 R<sup>31</sup> represents an optional substituent selected from halo, C<sub>1-4</sub> alkyl (which group is optionally substituted by one or more halo group), N(R<sup>32</sup>)R<sup>33</sup>, OR<sup>34</sup> or SR<sup>35</sup>;

R<sup>32</sup> and R<sup>33</sup> independently represent H, C<sub>1-4</sub> alkyl or C(O)R<sup>36</sup>;

R<sup>34</sup>, R<sup>35</sup> and R<sup>36</sup> independently represent H or C<sub>1-4</sub> alkyl; and

10 one of D<sup>1</sup> and D<sup>2</sup> represents H, and the other represents H, OR<sup>a</sup>, NHR<sup>a</sup>, C(=X<sup>11</sup>)X<sup>12</sup>R<sup>b</sup>, or D<sup>1</sup> and D<sup>2</sup> together represent a structural fragment of formula IVa:-



IVa

R<sup>a</sup> represents H or -A<sup>5</sup>[X<sup>14</sup>]<sub>n</sub>[C(O)],R<sup>c</sup>;

15 R<sup>b</sup> represents -A<sup>5</sup>[X<sup>14</sup>]<sub>n</sub>[C(O)],R<sup>c</sup>;

A<sup>5</sup> represents, at each occurrence, a single bond or C<sub>1-12</sub> alkylene (which alkylene group is optionally interrupted by one or more O, S(O)<sub>m</sub> and/or

- N(R<sup>f</sup>) group, and is optionally substituted by one or more of halo, OH, N(H)C(O)R<sup>g</sup>, C(O)N(R<sup>g</sup>)R<sup>h</sup>, C<sub>3-7</sub>-cycloalkyl (which cycloalkyl group is optionally interrupted by one or more O, S(O)<sub>m</sub> and/or N(R<sup>f</sup>) group and/or is optionally substituted by one or more substituents selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, halo, =O or =S), Het and C<sub>6-10</sub> aryl (which aryl and Het groups are themselves optionally substituted by one or more substituents selected from C<sub>1-6</sub> alkyl (optionally substituted by one or more halo substituent), C<sub>1-6</sub> alkoxy, halo, cyano, C(O)OR<sup>g</sup>, C(O)N(R<sup>g</sup>)R<sup>h</sup> and N(R<sup>f</sup>)R<sup>g</sup>);
- 5 R<sup>c</sup> and R<sup>d</sup> both represent H; or one of R<sup>c</sup> and R<sup>d</sup> represents H or C<sub>1-7</sub> alkoxy and the other represents C<sub>1-7</sub> alkyl (which alkyl group is optionally interrupted by one or more O atoms); or R<sup>c</sup> and R<sup>d</sup> together represent C<sub>3-8</sub> cycloalkyl, which cycloalkyl group is interrupted by one or more O, S(O)<sub>m</sub> and/or N(R<sup>f</sup>) group;
- 10 R<sup>e</sup> represents, at each occurrence, H, C<sub>1-12</sub> alkyl (which alkyl group is optionally interrupted by one or more O, S(O)<sub>m</sub> and/or N(R<sup>f</sup>) group, and/or is optionally substituted by one or more substituents selected from halo, OH, N(H)C(O)R<sup>g</sup> and C(O)N(R<sup>g</sup>)R<sup>h</sup>), A<sup>7</sup>-C<sub>3-7</sub>-cycloalkyl (which cycloalkyl group is optionally interrupted by one or more O, S(O)<sub>m</sub> and/or N(R<sup>f</sup>) group and/or is substituted by one or more substituents selected from C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, halo, =O and =S), A<sup>7</sup>-C<sub>6-10</sub> aryl or A<sup>7</sup>-Het (which aryl and Het groups are optionally substituted by one or more substituents selected from C<sub>1-6</sub> alkyl (optionally substituted by one or more halo substituent), C<sub>1-6</sub> alkoxy, halo, cyano, C(O)OR<sup>g</sup>, C(O)N(R<sup>g</sup>)R<sup>h</sup> and N(R<sup>f</sup>)R<sup>g</sup>);
- 15 A<sup>7</sup> represents a single bond or C<sub>1-7</sub> alkylene (which alkylene group is optionally interrupted by one or more O, S(O)<sub>m</sub> and/or N(R<sup>f</sup>) group, and/or are optionally substituted by one or more of halo, OH, N(H)COR<sup>g</sup> and CON(R<sup>g</sup>)R<sup>h</sup>);

Het represents, at each occurrence, a five- to ten-membered heteroaryl group, which may be aromatic in character, containing one or more nitrogen, oxygen or sulphur atoms in the ring system;

n and r independently represent 0 or 1;

5 X<sup>11</sup>, X<sup>12</sup> and X<sup>14</sup> independently represent O or S;

X<sup>13</sup> represents O or N(R<sup>f</sup>);

R<sup>f</sup> represents, at each occurrence, H, C<sub>1-4</sub> alkyl or C(O)R<sup>g</sup>;

R<sup>g</sup> and R<sup>h</sup> independently represent, at each occurrence, H or C<sub>1-4</sub> alkyl;

and

10

m represents, at each occurrence, 0, 1 or 2;

or a pharmaceutically acceptable salt thereof;

15 provided that:

(a) A and E do not both represent O or S;

(b) E and D do not both represent O or S;

(c) when R<sup>1</sup> represents OR<sup>1d</sup> and X<sub>1</sub> represents -C(O)-Z-A<sup>1</sup>,

-Z-CH<sub>2</sub>-S(O)<sub>m</sub>-A<sup>2</sup>- or -Z-C(O)-Z-A<sup>2</sup>, then A<sup>1</sup> or A<sup>2</sup> (as appropriate) do not represent a single bond;

20 (f) when X<sub>4</sub> represents -CH(R<sup>23</sup>)-, R<sup>1</sup> does not represent OH;

(g) when A<sup>5</sup> represents a single bond, then n and r both represent 0;

(f) when A<sup>5</sup> represents C<sub>1-12</sub> alkylene, then n represents 1;

(g) when A<sup>5</sup> represents -CH<sub>2</sub>-, n is 1 and r is 0, then R<sup>c</sup> does not represent

25 H; and

(h) the compound is not:-

(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Pro-Pab;

(R)- or (S)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Pro-Pab;

(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

- (*R*)- or (*S*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab;  
1-hydroxy-5-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;  
1-hydroxy-5,7-dimethyltetralin-1-yl-C(O)-Aze-Pab x HOAc;  
1-hydroxy-7-aminotetralin-1-yl-C(O)-Aze-Pab x HOAc;
- 5 1-hydroxytetralin-1-yl-C(O)-Aze-Pab x HOAc;  
7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;  
(*R*)- or (*S*)-7-methoxy-1-methyltetralin-1-yl-C(O)-Aze-Pab;  
4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab x OAc;  
(*S*)- or (*R*)-1-hydroxy-4-methoxyindan-1-yl-C(O)-Aze-Pab;
- 10 1-hydroxy-5-methoxytetralin-1-yl-C(O)-Aze-Pab(OH);  
(*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(OH);  
4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab(OH);  
4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab(OMe);  
(*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-
- 15 (*C*(O)OCH<sub>2</sub>CCl<sub>3</sub>);  
(*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-  
(*C*(O)OCH<sub>2</sub>CH<sub>3</sub>);  
7-methoxy-1-allyltetralin-1-yl-C(O)-Aze-Pab x HOAc;  
(*S*)- or (*R*)-1-hydroxy-7-chlorotetralin-1-yl-C(O)-Pro-Pab;
- 20 1-*n*-propyl-7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;  
6-chloro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
6,8-dichloro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
6-fluoro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;
- 25 4-hydroxy-6-methylchroman-4-yl-C(O)-Aze-Pab x HOAc;  
8-chloro-4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
6-chloro-4-hydroxy-8-methylchroman-4-yl-C(O)-Aze-Pab x HOAc;  
(*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-*i*-Pr);  
(*S*)- or (*R*)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-Et);

(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-Ch);

(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-allyl);

(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-Bzl);

(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-

5 (CO-O-methallyl);

1-hydroxy-7-aminotetralin-1-yl-C(O)-Aze-Pab(OH);

(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-Val);

(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-(Me)Pab; or

9-hydroxyfluoren-9-yl-C(O)-Aze-Pab x HOAc.

10

2. A compound as claimed in Claim 1 wherein R<sup>1</sup> represents OH or C<sub>1-4</sub> alkyl (which latter group is optionally substituted by cyano or OH).

15

3. A compound as claimed in any one of the preceding claims wherein R<sub>x</sub> represents a structural fragment of formula IIa or IIb.

20

4. A compound as claimed in any one of the preceding claims wherein, when R<sub>x</sub> represents a structural fragment of formula IIa, then the dotted lines represent bonds, A and E both represent CH and D represents -CH=CH-;

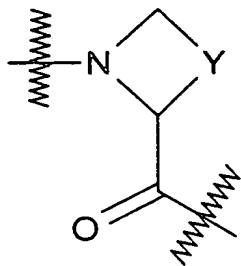
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5. A compound as claimed in any one of the preceding claims wherein, when R<sub>x</sub> represents a structural fragment of formula IIa, X<sub>1</sub> represents optionally unsaturated C<sub>2</sub>- or C<sub>3</sub>-alkylene, or -Z-A<sup>3</sup> (in which Z represents O, S(O)<sub>m</sub> or N(R<sup>25</sup>) (in which R<sup>25</sup> is as defined in Claim 1 or represents C<sub>1-4</sub> alkyl or C(O)R<sup>30</sup> and m and R<sup>30</sup> are as defined in Claim 1) and A<sup>3</sup> represents C<sub>1</sub>- or C<sub>2</sub>-alkylene (which latter group is optionally unsaturated)).

6. A compound as claimed in any one of the preceding claims wherein Y represents  $\text{CH}_2$ ,  $(\text{CH}_2)_2$  or  $(\text{CH}_2)_3$ .
7. A compound as claimed in any one of the preceding claims wherein B represents a structural fragment of formula IIIa in which  $X^5$ ,  $X^6$ ,  $X^7$  and  $X^8$  all represent CH.
8. A compound as claimed in any one of the preceding claims wherein, when  $D^1$  and  $D^2$  together represent a structural fragment of formula IVa, in which  $X^{13}$  is O, then one of  $R^c$  and  $R^d$  represents H or  $C_{1-7}$  alkoxy and the other represents  $C_{1-7}$  alkyl.
9. A compound as claimed in any one of Claims 1 to 7, wherein, when  $D^1$  or  $D^2$  represents  $\text{OR}^a$  and  $R^a$  represents  $-A^5[X^{14}]_n[\text{C}(\text{O})]_rR^e$ , and
- 15 (i)  $A^5$  is a single bond, then  $R^e$  is:-
- (1)  $A^7$ -aryl, optionally substituted by one or more halo,  $C_{1-6}$  alkoxy,  $C_{1-6}$  alkyl or halo- $C_{1-6}$ -alkyl substituents; or
  - (2) H or linear, branched, optionally unsaturated, and/or cyclic,  $C_{1-12}$  alkyl, which cyclic alkyl group is optionally interrupted by an O atom and, optionally, a further O atom or  $S(\text{O})_m$  group; or when
- 20 (ii)  $A^5$  is linear or branched  $C_{1-12}$  alkylene,  $X^{14}$  is O and r is 0, then  $R^e$  is  $C_{1-3}$  alkyl or  $A^7$ -aryl, in which  $A^7$  is a single bond.
10. A compound as claimed in any one of Claims 1 to 7 or 9, wherein, when  $D^1$  or  $D^2$  represents  $\text{OR}^a$ , then  $R^a$  is H or  $C_{1-4}$  alkyl.
11. A compound as claimed in any one of Claims 1 to 7, wherein, when  $D^1$  or  $D^2$  represents  $-\text{C}(=\text{X}^{11})\text{X}^{12}\text{R}^b$ , in which  $X^{11}$  represents O and  $X^{12}$  represents O or S, and, in which  $\text{R}^b$  group,  $A^5$  represents a single bond.

then R<sup>c</sup> represents optionally unsaturated C<sub>1-6</sub> alkyl, A<sup>7</sup>-C<sub>6-10</sub>-aryl (in which A<sup>7</sup> represents a single bond or C<sub>1-2</sub> alkylene, and which A<sup>7</sup>-C<sub>6-10</sub>-aryl group is optionally substituted by one or more halo, C<sub>1-4</sub> alkyl and/or C<sub>1-4</sub> alkoxy groups), or A<sup>7</sup>-C<sub>3-7</sub>-cycloalkyl, in which A<sup>7</sup> represents a single bond or linear or branched C<sub>1-7</sub> alkylene, and which cycloalkyl group is optionally substituted by C<sub>1-3</sub> alkyl.

12. A compound of formula I, as defined in any one of the preceding claims, wherein the fragment



10

is in the S-configuration.

13. A pharmaceutical formulation including a compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

14. A compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, for use as a pharmaceutical.

20 15 A compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition where inhibition of thrombin is required.

25 16. A compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, for use in the treatment of.

thrombosis.

17. A compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, for use as an anticoagulant.

5

18. The use of a compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, as active ingredient in the manufacture of a medicament for the treatment of a condition where inhibition of thrombin is required.

10

19. The use as claimed in Claim 18, wherein the condition is thrombosis.

20. The use of a compound as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, as active ingredient in the  
15 manufacture of an anticoagulant.

21. A method of treatment of a condition where inhibition of thrombin is required which method comprises administration of a therapeutically effective amount of a compound as defined in any one of Claims 1 to 12,  
20 or a pharmaceutically acceptable salt thereof, to a person suffering from, or susceptible to, such a condition.

22. A method as claimed in Claim 21, wherein the condition is thrombosis.

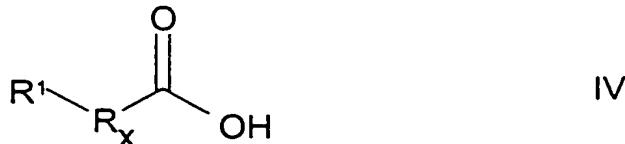
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23. A method as claimed in Claim 21, wherein the condition is hypercoagulability in blood and tissues.  
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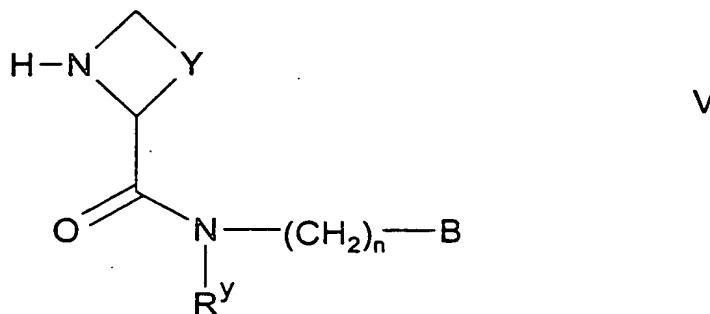
24. A process for the preparation of compounds of formula I which

comprises:

(i) the coupling of a compound of formula IV,

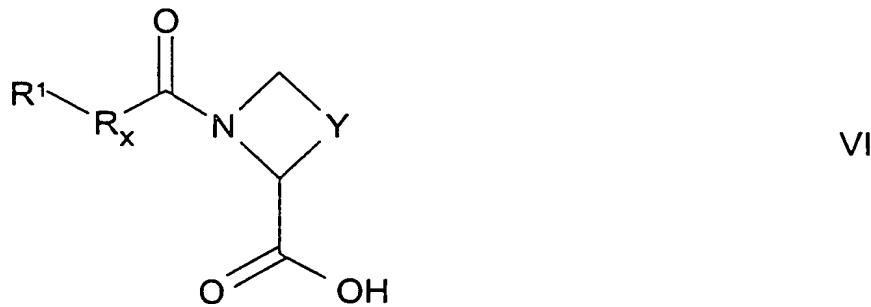


wherein R<sup>1</sup> and R<sub>x</sub> are as defined in Claim 1 with a compound of formula  
5 V,



wherein R<sup>y</sup>, Y, n and B are as defined in Claim 1;

(ii) the coupling of a compound of formula VI,

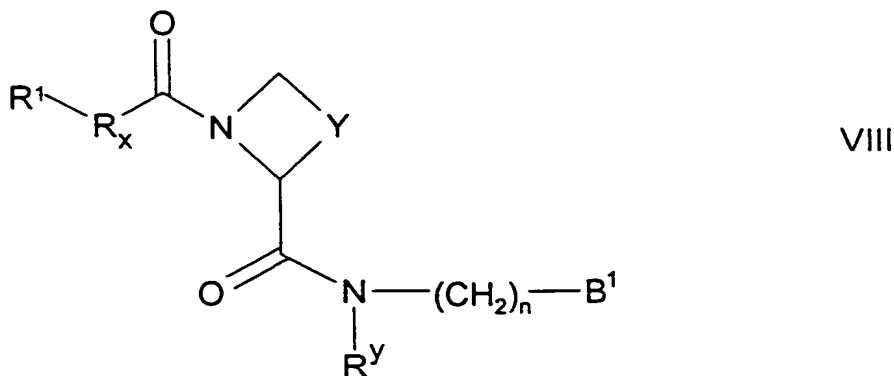


10 wherein R<sup>1</sup>, R<sub>x</sub> and Y are as defined in Claim 1 with a compound of formula VII,

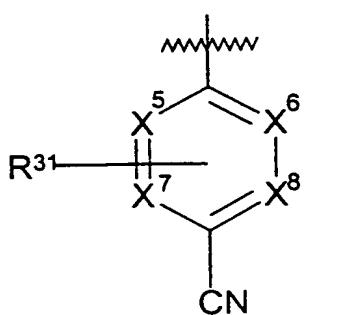


wherein R<sup>y</sup>, n and B are as defined in Claim 1;

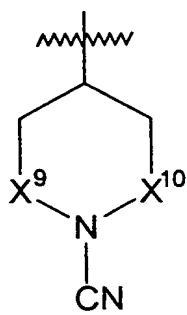
(iii) for compounds of formula I in which D<sup>1</sup> or D<sup>2</sup> represents OR<sup>a</sup> or  
15 NHR<sup>a</sup>, reaction of a compound of formula VIII,



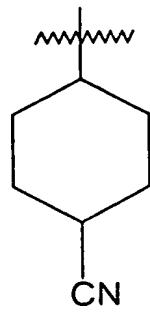
wherein  $B^1$  represents a structural fragment of formula IIId, IIIe or IIIf



III d



III e



III f

and  $R^1$ ,  $R_x$ ,  $Y$ ,  $R^y$ ,  $n$ ,  $R^{31}$ ,  $X^5$ ,  $X^6$ ,  $X^7$ ,  $X^8$ ,  $X^9$  and  $X^{10}$  are as defined in

5 Claim 1 with a compound of formula IX,



wherein  $X^a$  represents O or NH and  $R^a$  is as defined in Claim 1;

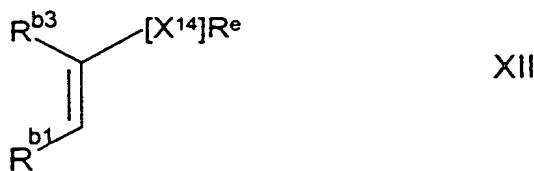
- (iv) for compounds of formula I in which  $D^1$  or  $D^2$  represents  $OR^a$  or  $NHR^a$ , reaction of a compound of formula I in which  $D^1$  or  $D^2$  (as appropriate) represents  $C(O)OR^{b1}$ , in which  $R^{b1}$  represents a protecting group with a compound of formula IX as defined above;
- (v) for compounds of formula I in which  $D^1$  or  $D^2$  represents  $OR^a$  or  $NHR^a$ ,  $R^a$  represents  $-A^5[X^{14}]_n[C(O)]_cR^e$ , in which  $A^5$  does not represent a single bond, and  $n$  represent 1, reaction of a compound of formula I in which  $D^1$  or  $D^2$  (as appropriate) represents OH or  $NH_2$ , with a compound

of formula X,



wherein  $L^1$  represents a suitable leaving group,  $A^{5a}$  represents  $A^5$ , as defined in Claim 1 except that it does not represent a single bond, and  $X^{14}$ , 5  $r$  and  $R^e$  are as defined in Claim 1;

- (vi) for compounds of formula I in which  $D^1$  or  $D^2$  represents  $OR^a$  or  $NHR^a$ ,  $R^a$  represents  $-A^5[X^{14}]_n[C(O)]_rR^e$ , in which  $A^5$  represents  $C_{2-12}$  alkylene, which alkylene group is branched at the carbon atom that is  $\alpha$  to the O or N atom of  $OR^a$  or  $NHR^a$  (as appropriate), and which group is 10 optionally branched at the carbon atom that is  $\beta$  to that atom,  $n$  represents 1,  $r$  represents 0 and  $R^e$  is as defined in Claim 1, reaction of a compound of formula I in which  $D^1$  or  $D^2$  (as appropriate) represents  $OH$  or  $NH_2$ , with a compound of formula XI,



- 15 or a geometrical isomer thereof, or a mixture of such geometrical isomers, in which  $R^{b1}$  and  $R^{b3}$  each represent H or an alkyl group, provided that the total number of carbon atoms provided by  $R^{b1}$  and  $R^{b3}$  does not exceed 10, and wherein  $X^{14}$  and  $R^e$  are as defined in Claim 1;

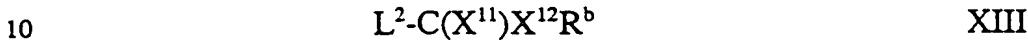
- (vii) for compounds of formula I in which  $D^1$  or  $D^2$  represents  $OR^a$  or 20  $NHR^a$ ,  $R^a$  represents  $-A^5[X^{14}]_n[C(O)]_rR^e$ , in which  $A^5$  represents a single bond, and  $R^e$  represents  $A^7-C_{3-6}$ -cycloalkyl, in which  $A^7$  represents a single bond, and the cycloalkyl group is interrupted by at least one O or S atom, which atom is between the carbon atom at the point of attachment to the O or NH group of  $OR^a$  or  $NHR^a$ , and a carbon atom that is  $\alpha$  to that 25 point of attachment, and which cycloalkyl group is optionally interrupted by one or more O or  $S(O)_m$  group and/or optionally substituted by one or

more =O group, reaction of a compound of formula I, in which D<sup>1</sup> or D<sup>2</sup> (as appropriate) represents OH or NH<sub>2</sub>, with a compound of formula XII,



wherein X<sup>15</sup> represents O or S and X<sup>16</sup> represents C<sub>1-4</sub> alkylene (which alkylene group is optionally interrupted by one or more O or S(O)<sub>m</sub> group and/or optionally substituted by one or more =O group);

(viii) for compounds of formula I in which D<sup>1</sup> or D<sup>2</sup> represents C(X<sup>11</sup>)X<sup>12</sup>R<sup>b</sup>, reaction of a compound of formula I in which D<sup>1</sup> and D<sup>2</sup> both represent H with a compound of formula XIII,



wherein L<sup>2</sup> represents a suitable leaving group, and X<sup>11</sup>, X<sup>12</sup> and R<sup>b</sup> are as defined in Claim 1;

(ix) for compounds of formula I in which D<sup>1</sup> and D<sup>2</sup> together represent a structural fragment of formula IVa, reaction of a corresponding compound of formula I in which D<sup>1</sup> or D<sup>2</sup> represents OH or NHR<sup>f</sup> (in which R<sup>f</sup> is as defined in Claim 1), with a compound of formula XV,



wherein R<sup>c1</sup> and R<sup>c2</sup> both represent -OR<sup>c3</sup>, in which R<sup>c3</sup> represents C<sub>1-3</sub> alkyl, or together represent =O, and R<sup>c</sup> and R<sup>d</sup> are as defined in Claim 1;

(x) for compounds of formula I in which one or more of X<sup>5</sup>, X<sup>6</sup>, X<sup>7</sup> and X<sup>8</sup> represent N-O, oxidation of a corresponding compound of formula I in which X<sup>5</sup>, X<sup>6</sup>, X<sup>7</sup> and/or X<sup>8</sup> (as appropriate) represent(s) N; or

(xi) for compounds of formula I in which any one of Z, X<sub>1</sub>, R<sup>2</sup>, R<sup>4</sup>, A<sup>5</sup>, A<sup>7</sup>, R<sup>c</sup>, R<sup>d</sup> and/or R<sup>e</sup> comprises or includes a S(O) or a S(O)<sub>2</sub> group, oxidation of a corresponding compound of formula I (or a compound corresponding to a compound of formula I) wherein Z, X<sub>1</sub>, R<sup>2</sup>, R<sup>4</sup>, A<sup>5</sup>, A<sup>7</sup>, R<sup>c</sup>, R<sup>d</sup> and/or R<sup>e</sup> (as appropriate) comprise(s) or include(s) a S group;

- (xii) for compounds of formula I in which D<sup>1</sup> and D<sup>2</sup> both represent H, removal of a OR<sup>a</sup>, NHR<sup>a</sup> or C(=X<sup>11</sup>)X<sup>12</sup>R<sup>b</sup> group (in which R<sup>a</sup>, R<sup>b</sup>, X<sup>11</sup> and X<sup>12</sup> are as defined in Claim 1), or removal of a structural fragment of formula IVa as defined in Claim 1, from a corresponding compound of  
5 formula I; or
- (xiii) introduction and/or interconversion of a substituent on an aromatic and/or non-aromatic, carbocyclic and/or heterocyclic ring in a corresponding compound of formula I.